UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,583	11/28/2000	Christiaan M. Saris	MBHB00-1213	9474

20306 7590 01/13/2004

MCDONNELL BOEHNEN HULBERT & BERGHOFF
300 SOUTH WACKER DRIVE
SUITE 3200
CHICAGO, IL 60606

EXAMINER	
MERTZ, PREMA MARIA	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 01/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,583	SARIS ET AL.	
	Examiner	Art Unit	
	Prema M Mertz	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,10,11,42-46 and 57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *57* is/are allowed.

6)☒ Claim(s) *1-8,10,11 and 42-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11/12/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/25/2003 has been entered.

Claims 9, 12-41, 47-56 have been canceled previously. Claims 1-8, 10-11, 42-46 and new claim 57 (11/25/2003), are under consideration.

2. Receipt of applicant's arguments and amendments filed in is acknowledged.

3. The following previous rejections and objections are withdrawn in light of applicants amendments filed in 11/25/2003:

(i) the rejection of claims 1-8, 10-1 1, 42-46, under 35 U.S.C. 102(a) as being anticipated by WO 9937662 (1999);

(ii) the rejection of claims 1-8, 10-1 1, 42-46 under 35 U.S.C. 102(b) as being anticipated by EPO855 404 A1 (1998); and

(iii) the rejection of claims 1-8, 10, 42 under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,075,222 (1991).

4. Applicant's arguments filed in 11/25/2003, have been fully considered but were persuasive in part. The issues remaining and new issues are stated below.

5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

6. The use of the trademark ATCC has been noted in this application. It should be capitalized whenever it appears and be accompanied by the ® symbol.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

7. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: Nucleic acid encoding an IL-1ra-R polypeptide.

Claim Rejections - 35 USC § 101

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 5-8, are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims embrace a host cell in the body of a transgenic animal, or a host cell in a gene therapy patient. Claim 5 encompasses human cells, fetuses and embryos, as well as non-human cells including animals, vertebrates, mammals, primates, chimeric animals, germ cells (including oocytes and sperm), fertilized eggs, fetal tissues and organs. Claim 8 is drawn to a method of producing such products. However, since it would that applicants do not intend to claim such human cells, amending the claims to require non-human host cells and the hand-of-man would obviate this rejection i.e. an isolated non-human mammalian host cell.

Claim Rejections - 35 USC § 112, first paragraph-new matter

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9a. Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1(d), recites "... no more than a 21% mismatch between the nucleotide sequences" which language is new matter in the claim, since the instant specification fails to disclose a mismatch of no more than 21%. The specification fails to provide proper support for this language in the claims for the following reason:

Page 23, lines 22-23, discloses that "by way of example, "moderately stringent conditions" of 50 C in 0.015 M sodium ion will allow about a 21% mismatch". However, instant claims 1(d), 2©, 3(e), encompass "no more than 21% mismatch". The specification does not disclose the "no more than 21% mismatch" as recited in the claim. The limitation as disclosed in the specification is not equivalent to the specific temperature recited in the claims. This rejection can only be obviated by reciting the specific mismatch for which there is support in the instant specification.

9b. Claims 1-8, 10-11, 42-46 are rejected under 35 U.S.C. 1 12, first paragraph.

This rejection is maintained for reasons of record set forth at pages 7-11 of the previous Office action (7/2/02) and set forth at pages 2-5 of the previous Office action (3/7/03).

Claims 1-8, 10-11, 42-46 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid encoding a polypeptide comprising the amino acid sequence set forth in SEQ ID NO:2, does not reasonably provide enablement for a nucleic acid that hybridizes to the complement of the nucleotide sequence of any of (a)-(c) allowing no more than a 21% mismatch, or a nucleic acid of SEQ ID NO:1 or the DNA insert in ATCC Deposit No. PTA-1423 encoding a polypeptide fragment "at least 25 amino acid residues" or a fragment of at least 16 nucleotides of SEQ ID NO:1.

The claimed genus of nucleic acid molecules encompasses variants of the nucleic acid molecule, however, the specification does not teach how to make a nucleic acid molecule encompassing these variants and encoding a polypeptide having an amino acid sequence less than SEQ ID NO:2. The specification only enables a nucleic acid molecule encoding a protein of amino acid sequence set forth in SEQ ID NO:2, and is not enabled for a nucleic acid molecule encompassed in claims 1(d), 2(a)-(c), 3(a)-(e).

The issue in the instant case is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. The recitation of "at least 25 amino acid residues..." in claim 2(a) for example, is not a sufficient structural limitation and broadly encompasses any nucleic acid molecule encoding a protein comprising 25 contiguous amino acid sequences of SEQ ID NO:2 and anything else as recited in the claims. Because of the presence of the term "of at least 25 amino acid residues" in claim 2(a), the claim encompasses a nucleic acid molecule encoding a polypeptide comprising any 25 contiguous amino acids from SEQ ID NO:2, and therefore the claim encompasses nucleic acid molecules

encoding polypeptide embodiments encompassing any other 127 amino acid sequences or more in addition to these 25 contiguous amino acids. The number of nucleic acid embodiments in this case are over 5×10^{100}. Similarly, a nucleic acid comprising a fragment of at least 16 nucleotides as recited in claim 2(b) encompasses over 5×10^{100} embodiments because the claim encompasses any 16 nucleotides of SEQ ID NO:1 and about 1000 nucleotides that are not present in SEQ ID NO:1.

Furthermore, Applicants have not taught how to make the instant nucleic acid molecules encoding polypeptides with the stretch of 25 contiguous amino acids as recited in claim 2(a). There is no guidance in the specification for how to make nucleic acid molecules encoding proteins having the amino acid sequences anything less than that disclosed in SEQ ID NO:2.

The instant claims are not limited to naturally-occurring compounds and the instant specification does not provide a description of a repeatable process of producing a nucleic acid molecule encoding a polypeptide comprising at least 25 contiguous amino acids of SEQ ID NO:2. To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination of those amino acid residues of the disclosed naturally-occurring protein, which are required for functional and structural integrity of those proteins. It is this additional characterization of the disclosed protein that is required in order to obtain the structural data needed to permit one to produce the claimed nucleic acid encoding a protein, which meets the structural requirements of the instant claims that constitutes undue experimentation.

Claims 4-8, 10-11, 42-46 are rejected under 35 U.S.C. 112, first paragraph insofar as they depend upon the above rejected claims for their limitations.

9c. Claims 2, 3-8, 10-11, 42-46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case only sets forth SEQ ID NO:1 and equivalent degenerative codon sequences thereof and therefore the written description is not commensurate in scope with the claims drawn to a nucleic acid comprising at least 16 nucleotides of SEQ ID NO:1 as recited in claim 2(b) or a nucleic acid encoding a polypeptide with at least one modification that is a conservative amino acid substitution, a C- or N- terminal truncation, wherein the polypeptide comprises at least 25 amino acid residues of SEQ ID NO:2 as recited in claim 3.

Claims 2 and 3 encompass a genus of nucleic acid molecules encoding polypeptides that comprise only portions of the full-length sequence encoding SEQ ID NO:2 as well as nucleic acid variants encoding proteins having one or more amino acid deletions made to the C- or N-terminal of SEQ ID NO:2. The specification and claims do not indicate what are the distinguishing attributes shared by the members of the genus for which the common portion is responsible for functional activity. The specification and claims do not place any limit on the number of amino acids that may be added to the portions since the claims are not limited to the full-length SEQ ID NO:2. Thus, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide a written description

as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural and functional attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, nucleic acid molecules encoding SEQ ID NO:2, alone are insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus.

Claims 4-8, 10-11, 42-46 are rejected under 35 U.S.C. 112, first paragraph insofar as they depend upon the above rejected claims for their limitations.

Applicants argue that the instant application explicitly teaches the nucleotide sequence and corresponding amino acid sequence for both human and murine IL-1ra-L polypeptide as well as 2 splice variants of the human sequence, and inherently discloses fragments that are merely portions of the specifically disclosed full-length sequences. However, contrary to Applicants arguments, the specification does not enable a nucleotide molecule encoding fragments of at least 25 amino acid residues as recited in claim 2, sub-part (a). In fact, the specification fails to exemplify any such nucleotide molecules encoding "subpeptides" within the meaning of this term. As written, claim 2, sub-parts (a)-(b), encompasses nucleic acid molecules encoding peptides of various lengths, and truncated peptides. Given the scope of the various nucleic acid molecules encoding peptides within this term i.e. the enormous number of peptide sequences possible, it is not evident that these resulting peptides would possess the desired activities. The

specification does not disclose which amino acids may be substituted, deleted, or inserted without affecting the functional activity of the factor nor reveals residues essential for activity. Without such guidance, the skilled artisan would have to obtain fragments by random amino acid alterations; however randomly substituting or deleting residues from a protein can inactivate the protein. Thus, it would require undue experimentation on the part of the skilled artisan to obtain nucleic acid molecules encoding amino acid sequences of the desired protein, which possesses the desired and favorable characteristics, in the absence of sufficient information to predict the results with an adequate degree of certainty.

The claimed invention encompasses nucleic acid molecules not envisioned or described in the specification, and neither does the specification disclose how these claimed DNA molecules can be distinguished from each other. The specification only enables nucleic acid molecules encoding proteins having the amino acid sequences shown in SEQ ID NO:2, the polypeptide having specific characteristics and properties. These properties may differ structurally, chemically and physically from other known proteins. By application of the factors set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) quantity of experimentation, (2) guidance presented, (3) the predictability of the art, and (4) the breadth of the claims, in the instant application, the quantity of experimentation to determine which other nucleic acid molecules encoding proteins having the desired activity, are encompassed by the scope of the claims is practically infinite and the guidance provided in the specification very little. Therefore, it would require undue experimentation to determine which nucleic acid molecules encoding proteins having the biological activity of a IL-1ra-R protein would be

encompassed by the scope of the claims. The disclosure of a single natural nucleic acid molecule of SEQ ID NO:1 is clearly insufficient support under the first paragraph of 35 U.S.C. § 112 for claims which encompass every and all nucleic acid molecules as recited in claim 2, including mutants thereof. In In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), the Courts have held that:

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since some improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that the scope of the claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

It is suggested that by employing conventional claim language, the claims be amended to recite the specific nucleic acid molecules supported by the instant specification.

9d. Claim 3-8, 10-11, 42-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid encoding a polypeptide

comprising the amino acid sequence set forth in SEQ ID NO:2, does not reasonably provide enablement for an isolated nucleic acid encoding a polypeptide which is at least 70% identical to to SEQ ID NO:2 The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 3, is overly broad in the recitation of "at least 70% identical to an amino acid sequence" since no guidance is provided as to which of the myriad of polynucleotide species encoding polypeptide species encompassed by the claim will retain the desired characteristics. Furthermore, the recitation of "at least one conservative amino acid substitution" encompasses one conservative amino acid substitution and other non-conservative amino acid substitutions. Applicants disclose that variants of the polynucleotide can be generated by conservative or nonconservative changes (page 24, lines 26-29). However, allelic, splice species or polymorphic variants can also lead to nucleic acid variants, and Applicants have failed to disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of SEQ ID NO:2 (page 25, lines 10-19). Moreover, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically

affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is no guidance provided in the specification as to how one of ordinary skill in the art would generate a nucleic acid sequence encoding a polypeptide other than that exemplified in the specification. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claims 4-8, 10-11, 42-46 are rejected under 35 U.S.C. 112, first paragraph insofar as they depend upon the above rejected claim for their limitations.

Applicants argue that the specification specifically discloses both SEQ ID NO:1 and SEQ ID NO:2, and the specification is enabling for fragments of these sequences, as such fragments are merely portions of the specifically disclosed sequences. Furthermore, Applicants argue that the claims recite polynucleotides that hybridize to the complement of the claimed nucleotide sequences under hybridization conditions allowing no more than a 21% mismatch between the nucleotide sequences and that one of skill in the art would be able to readily discern whether there was a greater than 21% mismatch between two nucleic acid molecules. Applicants also argue that the specification provides one of skill in the art with guidelines for preparing a polypeptide having one or more conservative substitutions such that the polypeptide encoded by the polynucleotide retains the functional and chemical characteristics of the IL-1ra-R polypeptides. (Table 1, pages 27-28; page 15; page 26). However, contrary to applicants arguments, the limitations with respect to claim 3 are directly analogous to those of claim 7 of U.S. Patent Number 4,703,008 which were held to be invalid under 35 U.S.C. § 112, first paragraph, for want of enablement in Amgen Inc. v. Chugai Pharmaceuticals Co. Ltd., 18 U.S.P.Q. 2d 1016, Fed. Cir. 1991 (see page 1026, section D). In that instance, a claim to a nucleic acid encoding a polypeptide having an amino acid sequence sufficiently duplicative of the amino acid sequence of erythropoietin (EPO) so as to have a specified biological activity was held to be invalid under 35 U.S.C. § 112, first paragraph, for want of enablement. This limitation is directly analogous to the "fragment" and "70% identical" limitations of instant claim 3. The disclosure upon which that claim was based described a recombinant DNA encoding

EPO and a few analogs thereof. That disclosure differs from the instant specification because, whereas the instant specification describes only one nucleic acid molecules encoding 1 protein, it does not describe even a single variant thereof. The court held that what is necessary to support claims of this breadth is a disclosure sufficient to enable one skilled in the art to carry out the invention commensurate with the scope of the claims. For amino acid sequences, that means disclosing how to make and use enough sequences to justify the grant of the claims sought. In other words, since it would require undue experimentation to identify nucleic acids encoding other 152 amino acid polypeptides, the entire scope of the claims is not enabled.

Furthermore, with respect to the "at least one conservative amino acid substitution" limitation, the instant specification does not outline residues which are considered conservative. This is not adequate guidance as to the nature of the analogues or variants of the nucleic acid molecules that may be constructed to produce the desired protein, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Furthermore, claim 3 does not indicate the number of conservative substitutions i.e. there is no upper limit to the amount of substitutions. Therefore, Applicants have not presented enablement commensurate in scope with the claims. Furthermore, the amount of embodiments corresponding to the desirable nucleic acid molecules, may be innumerable, and the enabled embodiments amount to only one. Therefore, there are substantial scientific reasons to doubt the scope of enablement, as set forth above. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe any other nucleic acid molecules encoding polypeptides other than that whose amino acid sequence is shown in SEQ ID NO:2, and since it is deemed to constitute undue experimentation to determine all the

others, the disclosure is not commensurate with the scope of the claims. Therefore, Applicants are not enabled for nucleic acid molecules encoding a protein having anything less than the amino acid sequence shown in SEQ ID NO:2.

Claim Rejections - 35 USC § 112, second paragraph

10. Claims 1-8, 10-1 1, 42-46 are rejected under 35 U.S.C. 1 12, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-3 have been amended to recite that the claimed nucleic acid molecule hybridizes to the complement of the nucleotide sequence of any of (a)-(c) under "hybridization conditions" allowing no more than a 21% mismatch between the nucleotide sequences. The claims are vague and indefinite. The specification on page 23, lines 22-23, recites that "by way of example", "moderately stringent conditions" of 50 C in 0.015 sodium ion will allow about a 21% mismatch. Therefore, since the conditions recited in the specification are exemplary, the hybridization condition is a relative and conditional term and renders the claims indefinite. The metes and bounds of the claims thus cannnot be ascertained.

Claim 3(a) recites "at least one conservative amino acid substitution". The claim is indefinite in the recitation of this term. This language is vague and indefinite since it encompasses potentially any one conservative amino acid substitution of the polypeptide without an upper limit on the number of conservative substitutions.

Similarly, with respect to the limitation "having a C- and/or N-terminal truncation" in claim 3(b), there is no upper limit on the number of amino acids that are deleted from the C and/or N terminus. Therefore the metes and bounds of the claim are indefinite.

Claims 4-8, 10-11, 42-46 are rejected as vague and indefinite insofar as they are dependent on claims 1-3 for their limitations.

Conclusion

Claim 57 is allowable.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Prema Mertz whose telephone number is (703) 308-4229. The examiner can normally be reached on Monday-Friday from 7:00AM to 3:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (703) 746-5300.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [yvonne.eyler@uspto.gov].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark Office on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Prema Mertz

Prema Mertz Ph.D.
Primary Examiner
Art Unit 1646
January 6, 2004